



## Clinical trial results:

### A Phase 3, Randomized, Parallel-Group, Multicenter, Open-Label, Pharmacokinetic, Noninferiority Study of Ravulizumab Administered Subcutaneously Versus Intravenously in Adult Patients With Paroxysmal Nocturnal Hemoglobinuria Currently Treated With Eculizumab

#### Summary

|                          |                                  |
|--------------------------|----------------------------------|
| EudraCT number           | 2017-002370-39                   |
| Trial protocol           | DE FR BE GB NL SE FI CZ ES AT IT |
| Global end of trial date | 31 August 2023                   |

#### Results information

|                                |                   |
|--------------------------------|-------------------|
| Result version number          | v2 (current)      |
| This version publication date  | 01 September 2024 |
| First version publication date | 25 August 2022    |
| Version creation reason        |                   |

#### Trial information

##### Trial identification

|                       |                  |
|-----------------------|------------------|
| Sponsor protocol code | ALXN1210-PNH-303 |
|-----------------------|------------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03748823 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Alexion Pharmaceuticals Inc.  |
| Sponsor organisation address | 121 Seaport Boulevard, Boston, United States, 02210   |
| Public contact               | European Clinical Trial Information, Alexion Europe SAS, +33 147100615, clinicaltrials.eu@alexion.com |
| Scientific contact           | European Clinical Trial Information, Alexion Europe SAS, +33 147100615, clinicaltrials.eu@alexion.com |

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                |
|--|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 31 August 2023 |
| Is this the analysis of the primary completion data? | No             |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 31 August 2023 |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate pharmacokinetics (PK) of ravulizumab administered subcutaneously via an on-body delivery system (OBDS) compared with intravenously administered ravulizumab in adult participants with Paroxysmal Nocturnal Hemoglobinuria (PNH) who are clinically stable on eculizumab for at least 6 months.

Protection of trial subjects:

This trial was conducted in compliance with Good Clinical Practice.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 05 March 2019 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Australia: 9           |
| Country: Number of subjects enrolled | Brazil: 25             |
| Country: Number of subjects enrolled | Canada: 1              |
| Country: Number of subjects enrolled | Austria: 4             |
| Country: Number of subjects enrolled | Belgium: 10            |
| Country: Number of subjects enrolled | Finland: 2             |
| Country: Number of subjects enrolled | France: 20             |
| Country: Number of subjects enrolled | Italy: 9               |
| Country: Number of subjects enrolled | Netherlands: 1         |
| Country: Number of subjects enrolled | Spain: 14              |
| Country: Number of subjects enrolled | Sweden: 1              |
| Country: Number of subjects enrolled | Russian Federation: 10 |
| Country: Number of subjects enrolled | Türkiye: 29            |
| Country: Number of subjects enrolled | United States: 1       |
| Worldwide total number of subjects   | 136                    |
| EEA total number of subjects         | 61                     |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 123 |
| From 65 to 84 years                       | 13  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Participants were stratified by weight group ( $\geq 40$  to  $< 60$  kg and  $\geq 60$  to  $< 100$  kg) and then randomized in a 2:1 ratio to 2 treatment groups.

### Period 1

|                              |                             |
|------------------------------|-----------------------------|
| Period 1 title               | Randomized Treatment Period |
| Is this the baseline period? | Yes                         |
| Allocation method            | Randomised - controlled     |
| Blinding used                | Not blinded                 |

### Arms

|                              |                                   |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes                               |
| <b>Arm title</b>             | Ravulizumab IV/SC Treatment Group |

Arm description:

During the Randomized Treatment Period, participants received a weight-based single loading dose (2400 to 2700 milligrams [mg]) of ravulizumab IV on Day 1, followed by a maintenance weight-based dose (3000 to 3300 mg) of ravulizumab IV on Day 15. During the Extension Period (Day 71 up to Day 1275), participants received 490 mg of ravulizumab SC once every week (qw).

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Ravulizumab           |
| Investigational medicinal product code | ALXN1210              |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

Participants received ALXN1210 at prespecified dose and timepoints.

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | Ravulizumab SC/SC Treatment Group |
|------------------|-----------------------------------|

Arm description:

During the Randomized Treatment Period, participants received a weight-based single loading dose (2400 to 2700 mg) of ravulizumab SC on Day 1, followed by maintenance weight-based doses (490 mg) of ravulizumab SC qw from Days 15 to 64. During the Extension Period (Day 71 up to Day 1275), participants received 490 mg of ravulizumab SC qw.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Ravulizumab           |
| Investigational medicinal product code | ALXN1210              |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Subcutaneous use      |

Dosage and administration details:

Participants received ALXN1210 at prespecified dose and timepoints.

| Number of subjects in period 1         | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |
|--|-----------------------------------|-----------------------------------|
| Started                                | 46                                | 90                                |
| Received at least 1 dose of study drug | 46                                | 90                                |
| Treated and not included in analysis   | 1 <sup>[1]</sup>                  | 6 <sup>[2]</sup>                  |
| Full Analysis Set                      | 45                                | 84                                |
| Safety Analysis Set                    | 45                                | 84                                |
| Completed                              | 44                                | 84                                |
| Not completed                          | 2                                 | 6                                 |
| Consent withdrawn by subject           | 1                                 | -                                 |
| Site Source Document Deviations        | 1                                 | 6                                 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Includes participants from 1 site with source documentation deviations and findings related to deficiencies in Investigator oversight. Participants were treated but not included in the analysis.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Includes participants from 1 site with source documentation deviations and findings related to deficiencies in Investigator oversight. Participants were treated but not included in the analysis.

## Period 2

|                              |                  |
|------------------------------|------------------|
| Period 2 title               | Extension Period |
| Is this the baseline period? | No               |
| Allocation method            | Not applicable   |
| Blinding used                | Not blinded      |

## Arms

|                              |                                   |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes                               |
| <b>Arm title</b>             | Ravulizumab IV/SC Treatment Group |

Arm description:

During the Randomized Treatment Period, participants received a weight-based single loading dose (2400 to 2700 milligrams [mg]) of ravulizumab IV on Day 1, followed by a maintenance weight-based dose (3000 to 3300 mg) of ravulizumab IV on Day 15. During the Extension Period (Day 72 up to Day 1275), participants received 490 mg of ravulizumab SC once every week (qw).

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Ravulizumab           |
| Investigational medicinal product code |                       |
| Other name                             | ALXN1210              |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

Participants received ALXN1210 at prespecified dose and timepoints.

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | Ravulizumab SC/SC Treatment Group |
|------------------|-----------------------------------|

Arm description:

During the Randomized Treatment Period, participants received a weight-based single loading dose (2400 to 2700 mg) of ravulizumab SC on Day 1, followed by maintenance weight-based doses (490 mg) of ravulizumab SC qw from Days 15 to 64. During the Extension Period (Day 72 up to Day 1275), participants received 490 mg of ravulizumab SC qw.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |                       |
|--|-----------------------|
| Investigational medicinal product name | Ravulizumab           |
| Investigational medicinal product code |                       |
| Other name                             | ALXN1210              |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Subcutaneous use      |

Dosage and administration details:

Participants received ALXN1210 at prespecified dose and timepoints.

| <b>Number of subjects in period 2<sup>[3]</sup></b> | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |
|---|-----------------------------------|-----------------------------------|
| Started   | 44                                | 83                                |
| Received at least 1 dose of study drug              | 44                                | 83                                |
| Treated but not included in the analysis            | 1 <sup>[4]</sup>                  | 6 <sup>[5]</sup>                  |
| Completed   | 31                                | 64                                |
| Not completed                                       | 13                                | 19                                |
| Adverse event, serious fatal                        | 2                                 | 2                                 |
| Consent withdrawn by subject                        | 9                                 | 12                                |
| Physician decision                                  | 1                                 | 2                                 |
| Other than Specified                                | -                                 | 1                                 |
| Lost to follow-up                                   | -                                 | 1                                 |
| Protocol deviation                                  | 1                                 | -                                 |
| Lack of efficacy                                    | -                                 | 1                                 |

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 44 participants that completed the randomized treatment period entered the extension period.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Includes participants from 1 site with source documentation deviations and findings related to deficiencies in Investigator oversight. Participants were treated but not included in the analysis.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Includes participants from 1 site with source documentation deviations and findings related to deficiencies in Investigator oversight. Participants were treated but not included in the analysis.

## Baseline characteristics

### Reporting groups

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Ravulizumab IV/SC Treatment Group |
|-----------------------|-----------------------------------|

Reporting group description:

During the Randomized Treatment Period, participants received a weight-based single loading dose (2400 to 2700 milligrams [mg]) of ravulizumab IV on Day 1, followed by a maintenance weight-based dose (3000 to 3300 mg) of ravulizumab IV on Day 15. During the Extension Period (Day 71 up to Day 1275), participants received 490 mg of ravulizumab SC once every week (qw).

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Ravulizumab SC/SC Treatment Group |
|-----------------------|-----------------------------------|

Reporting group description:

During the Randomized Treatment Period, participants received a weight-based single loading dose (2400 to 2700 mg) of ravulizumab SC on Day 1, followed by maintenance weight-based doses (490 mg) of ravulizumab SC qw from Days 15 to 64. During the Extension Period (Day 71 up to Day 1275), participants received 490 mg of ravulizumab SC qw.

| Reporting group values                             | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group | Total |
|--|-----------------------------------|-----------------------------------|-------|
| Number of subjects                                 | 46                                | 90                                | 136   |
| Age categorical                                    |                                   |                                   |       |
| Units: Subjects                                    |                                   |                                   |       |
| In utero   | 0                                 | 0                                 | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0                                 | 0                                 | 0     |
| Newborns (0-27 days)                               | 0                                 | 0                                 | 0     |
| Infants and toddlers (28 days-23 months)           | 0                                 | 0                                 | 0     |
| Children (2-11 years)                              | 0                                 | 0                                 | 0     |
| Adolescents (12-17 years)                          | 0                                 | 0                                 | 0     |
| Adults (18-64 years)                               | 42                                | 79                                | 121   |
| From 65-84 years                                   | 4                                 | 11                                | 15    |
| 85 years and over                                  | 0                                 | 0                                 | 0     |
| Age Continuous                                     |                                   |                                   |       |
| Units: years                                       |                                   |                                   |       |
| arithmetic mean                                    | 46.4                              | 45.3                              | -     |
| standard deviation                                 | ± 13.22                           | ± 14.47                           | -     |
| Sex: Female, Male                                  |                                   |                                   |       |
| Units: participants                                |                                   |                                   |       |
| Female   | 25                                | 47                                | 72    |
| Male   | 21                                | 43                                | 64    |
| Race (NIH/OMB)                                     |                                   |                                   |       |
| Units: Subjects                                    |                                   |                                   |       |
| American Indian or Alaska Native                   | 1                                 | 0                                 | 1     |
| Asian  | 2                                 | 0                                 | 2     |
| Native Hawaiian or Other Pacific Islander          | 0                                 | 0                                 | 0     |
| Black or African American                          | 4                                 | 5                                 | 9     |
| White  | 30                                | 67                                | 97    |
| More than one race                                 | 2                                 | 4                                 | 6     |
| Unknown or Not Reported                            | 7                                 | 14                                | 21    |
| Ethnicity (NIH/OMB)                                |                                   |                                   |       |
| Units: Subjects                                    |                                   |                                   |       |

|                         |    |    |    |
|-------------------------|----|----|----|
| Hispanic or Latino      | 7  | 19 | 26 |
| Not Hispanic or Latino  | 29 | 53 | 82 |
| Unknown or Not Reported | 10 | 18 | 28 |

## End points

### End points reporting groups

|  |                                   |
|--|-----------------------------------|
| Reporting group title  | Ravulizumab IV/SC Treatment Group |
| Reporting group description:<br>During the Randomized Treatment Period, participants received a weight-based single loading dose (2400 to 2700 milligrams [mg]) of ravulizumab IV on Day 1, followed by a maintenance weight-based dose (3000 to 3300 mg) of ravulizumab IV on Day 15. During the Extension Period (Day 71 up to Day 1275), participants received 490 mg of ravulizumab SC once every week (qw). |                                   |
| Reporting group title  | Ravulizumab SC/SC Treatment Group |
| Reporting group description:<br>During the Randomized Treatment Period, participants received a weight-based single loading dose (2400 to 2700 mg) of ravulizumab SC on Day 1, followed by maintenance weight-based doses (490 mg) of ravulizumab SC qw from Days 15 to 64. During the Extension Period (Day 71 up to Day 1275), participants received 490 mg of ravulizumab SC qw.                              |                                   |
| Reporting group title  | Ravulizumab IV/SC Treatment Group |
| Reporting group description:<br>During the Randomized Treatment Period, participants received a weight-based single loading dose (2400 to 2700 milligrams [mg]) of ravulizumab IV on Day 1, followed by a maintenance weight-based dose (3000 to 3300 mg) of ravulizumab IV on Day 15. During the Extension Period (Day 72 up to Day 1275), participants received 490 mg of ravulizumab SC once every week (qw). |                                   |
| Reporting group title  | Ravulizumab SC/SC Treatment Group |
| Reporting group description:<br>During the Randomized Treatment Period, participants received a weight-based single loading dose (2400 to 2700 mg) of ravulizumab SC on Day 1, followed by maintenance weight-based doses (490 mg) of ravulizumab SC qw from Days 15 to 64. During the Extension Period (Day 72 up to Day 1275), participants received 490 mg of ravulizumab SC qw.                              |                                   |

### Primary: Ctrough Serum Concentration of Ravulizumab

|  |  |
|--|--|
| End point title  | Ctrough Serum Concentration of Ravulizumab |
| End point description:<br>Pharmacokinetic (PK) analysis set included all participants who had evaluable PK data. |  |
| End point type   | Primary                                    |
| End point timeframe:<br>Predose at Day 71  |  |

| End point values                     | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|--------------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                   | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed          | 43                                | 70                                |  |  |
| Units: microgram/milliliter (µg/mL)  |                                   |                                   |  |  |
| arithmetic mean (standard deviation) | 457.58 (± 108.491)                | 578.70 (± 140.819)                |  |  |

### Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Statistical analysis 1  |
| Comparison groups                       | Ravulizumab IV/SC Treatment Group v Ravulizumab SC/SC Treatment Group |
| Number of subjects included in analysis | 113   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           |   |
| P-value                                 | < 0.0001 <sup>[1]</sup>   |
| Method                                  | ANOVA   |
| Parameter estimate                      | Ratio of Geometric Least Squares Mean                                 |
| Point estimate                          | 1.257   |
| Confidence interval                     |   |
| level                                   | 90 %  |
| sides                                   | 2-sided   |
| lower limit                             | 1.16  |
| upper limit                             | 1.361   |

Notes:

[1] - Analysis of variance (ANOVA) was performed on log-transformed Ctrough and included treatment and stratified weight group as fixed effects.

### Secondary: Ctrough Serum Concentration of Ravulizumab at Day 351

|                        |   |
|------------------------|---|
| End point title        | Ctrough Serum Concentration of Ravulizumab at Day 351   |
| End point description: | SC treated full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab SC, and were not excluded from analysis. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure. |
| End point type         | Secondary   |
| End point timeframe:   |   |
| Predose at Day 351     |   |

| End point values                     | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|--------------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                   | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed          | 34                                | 74                                |  |  |
| Units: µg/mL                         |                                   |                                   |  |  |
| arithmetic mean (standard deviation) | 712.79 (± 203.180)                | 737.65 (± 208.894)                |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Free Serum Complement Component 5 (C5) Concentrations at Day 71

|                        |   |
|------------------------|---|
| End point title        | Free Serum Complement Component 5 (C5) Concentrations at Day 71   |
| End point description: | Pharmacodynamic (PD) analysis set included all participants who received at least 1 dose of ravulizumab and who had evaluable PD data. Here, Number of Participants Analyzed signifies those participants who |

were evaluable for this outcome measure.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Predose at Day 71    |           |

| End point values                     | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|--------------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                   | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed          | 44                                | 83                                |  |  |
| Units: µg/mL                         |                                   |                                   |  |  |
| arithmetic mean (standard deviation) | 0.072193 (± 0.0245225)            | 0.059458 (± 0.0182180)            |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Free Serum Complement Component 5 (C5) Concentrations at Day 351

|                 |  |
|-----------------|--|
| End point title | Free Serum Complement Component 5 (C5) Concentrations at Day 351 |
|-----------------|--|

End point description:

SC treated full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab SC, and were not excluded from analysis. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Predose at Day 351   |           |

| End point values                     | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|--------------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                   | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed          | 33                                | 73                                |  |  |
| Units: µg/mL                         |                                   |                                   |  |  |
| arithmetic mean (standard deviation) | 0.071627 (± 0.0227980)            | 0.069711 (± 0.0208784)            |  |  |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Change From Baseline in Lactate Dehydrogenase (LDH) Levels at Day 71

|                 |  |
|-----------------|--|
| End point title | Percent Change From Baseline in Lactate Dehydrogenase (LDH) Levels at Day 71 |
|-----------------|--|

End point description:

Baseline was defined as the last assessment prior to first study drug dose. Lactate dehydrogenase samples impacted by tabletop hemolysis were excluded from the analysis. Full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab, and were not excluded from analysis. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Day 71

| End point values                     | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|--------------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                   | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed          | 43                                | 82                                |  |  |
| Units: percent change                |                                   |                                   |  |  |
| arithmetic mean (standard deviation) | 5.73 ( $\pm$ 29.716)              | 2.57 ( $\pm$ 33.883)              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Subscale Version 4 Score at Day 71

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Subscale Version 4 Score at Day 71 |
|-----------------|---|

End point description:

FACIT-fatigue subscale is a 13-item questionnaire that assesses self-reported fatigue and its impact upon daily activities and function over the preceding 7 days. Items are scored on a 5 point Likert-type scale. Item scores ranged from 0 ("not at all") to 4 ("very much"). The total, summed score ranged from 0 to 52; lower scores indicating greater fatigue and higher score indicating better health-related quality of life. Baseline was defined as the last non-missing value prior to the first dose of study drug. Full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab, and were not excluded from analysis. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Day 71

| End point values                     | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|--------------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                   | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed          | 44                                | 80                                |  |  |
| Units: units on a scale              |                                   |                                   |  |  |
| arithmetic mean (standard deviation) | -0.83 ( $\pm$ 7.378)              | 1.21 ( $\pm$ 7.882)               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change From Baseline in Lactate Dehydrogenase Levels at Day 351

|   |   |
|---|---|
| End point title   | Percent Change From Baseline in Lactate Dehydrogenase Levels at Day 351 |
| End point description:<br>Subcutaneous baseline was defined as the last assessment prior to first dose of subcutaneous treatment. Lactate dehydrogenase samples impacted by tabletop hemolysis were excluded from the analysis. SC treated full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab SC, and were not excluded from analysis. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Baseline, Day 351   |   |

| End point values                     | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|--------------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                   | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed          | 34                                | 73                                |  |  |
| Units: percent change                |                                   |                                   |  |  |
| arithmetic mean (standard deviation) | -0.83 ( $\pm$ 17.225)             | 1.74 ( $\pm$ 21.905)              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue Scale Version 4 Score at Day 351

|  |  |
|--|--|
| End point title  | Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue Scale Version 4 Score at Day 351 <sup>[2]</sup> |
| End point description:<br>FACIT-fatigue subscale is a 13-item questionnaire that assesses self-reported fatigue and its impact |  |

upon daily activities and function over the preceding 7 days. Items are scored on a 5 point Likert-type scale. Item scores ranged from 0 ("not at all") to 4 ("very much"). The total, summed score ranged from 0 to 52; lower scores indicating greater fatigue and higher score indicating better health-related quality of life. Baseline was defined as the last non-missing value prior to the first dose of subcutaneous treatment. SC treated full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab SC, and were not excluded from analysis. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure. This outcome measure was planned to be reported for ravulizumab SC/SC treatment group only.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Day 351

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This outcome measure was planned to be reported for ravulizumab SC/SC treatment group only.

| End point values                     | Ravulizumab SC/SC Treatment Group |  |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type                   | Reporting group                   |  |  |  |
| Number of subjects analysed          | 70                                |  |  |  |
| Units: units on a scale              |                                   |  |  |  |
| arithmetic mean (standard deviation) | 2.57 (± 7.178)                    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Treatment Administration Satisfaction Questionnaire (TASQ) Score at Day 71

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Treatment Administration Satisfaction Questionnaire (TASQ) Score at Day 71 |
|-----------------|--|

End point description:

TASQ is a validated questionnaire that assesses participants' perceptions and satisfaction with ravulizumab treatment administration routes, which included 5 domains: physical impact, psychological impact, impact on activities of daily living, convenience, and satisfaction. Each domain offers up to 5 response options with lower scores indicating a more positive response; scoring is completed by summing each of the 5 domains. Baseline was defined as the last non-missing value prior to the first dose of study drug. Full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab, and were not excluded from analysis. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Day 71

| End point values                     | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|--------------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                   | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed          | 43                                | 78                                |  |  |
| Units: units on a scale              |                                   |                                   |  |  |
| arithmetic mean (standard deviation) | -7.00 ( $\pm$ 34.581)             | -70.54 ( $\pm$ 70.522)            |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Treatment Administration Satisfaction Questionnaire (TASQ) Score at Day 351

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Treatment Administration Satisfaction Questionnaire (TASQ) Score at Day 351 <sup>[3]</sup> |
|-----------------|--|

End point description:

TASQ is a validated questionnaire that assesses participants' perceptions and satisfaction with ravulizumab treatment administration routes, which included 5 domains: physical impact, psychological impact, impact on activities of daily living, convenience, and satisfaction. Each domain offers up to 5 response options with lower scores indicating a more positive response; scoring is completed by summing each of the 5 domains. Baseline was defined as the last non-missing value prior to the first dose of subcutaneous treatment. SC treated full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab SC, and were not excluded from analysis. Here, Number of Participants analyzed signifies those participants who were evaluable for this outcome measure. This outcome measure was planned to be reported for ravulizumab SC/SC treatment group only.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Day 351

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This outcome measure was planned to be reported for ravulizumab SC/SC treatment group only.

| End point values                     | Ravulizumab SC/SC Treatment Group |  |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type                   | Reporting group                   |  |  |  |
| Number of subjects analysed          | 72                                |  |  |  |
| Units: units on a scale              |                                   |  |  |  |
| arithmetic mean (standard deviation) | -69.29 ( $\pm$ 80.068)            |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Who Experienced Breakthrough Hemolysis up

**to Day 71**

|  |  |
|--|--|
| End point title  | Percentage of Participants Who Experienced Breakthrough Hemolysis up to Day 71 |
| End point description:<br>Breakthrough hemolysis was defined as at least one new or worsening symptom or sign of intravascular hemolysis (fatigue, hemoglobinuria, abdominal pain, shortness of breath [dyspnea], anemia [hemoglobin <10 grams/deciliter (g/dL)], major adverse vascular event [MAVE, including thrombosis], dysphagia, or erectile dysfunction) in the presence of elevated LDH $\geq 2 \times$ upper limit of normal (ULN). Denominator for a percentage was participants with at least one post-baseline data for the period. For Through Day 71, only visits with data were used to assess breakthrough hemolysis. Full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab, and were not excluded from analysis. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Baseline up to Day 71  |  |

| End point values                  | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|-----------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed       | 45                                | 84                                |  |  |
| Units: percentage of participants |                                   |                                   |  |  |
| number (confidence interval 95%)  | 2.2 (0.06 to 11.77)               | 1.2 (0.03 to 6.46)                |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Percentage of Participants Who Experienced Breakthrough Hemolysis up to Day 351**

|  |   |
|--|---|
| End point title  | Percentage of Participants Who Experienced Breakthrough Hemolysis up to Day 351 |
| End point description:<br>Breakthrough hemolysis was defined as at least one new or worsening symptom or sign of intravascular hemolysis (fatigue, hemoglobinuria, abdominal pain, shortness of breath [dyspnea], anemia [hemoglobin <10 g/dL], major adverse vascular event [MAVE, including thrombosis], dysphagia, or erectile dysfunction) in the presence of elevated LDH $\geq 2 \times$ ULN. Denominator for a percentage was participants with at least one post-baseline data for the period. SC treated full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab SC, and were not excluded from analysis. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Baseline up to Day 351   |   |

| End point values                  | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|-----------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed       | 44                                | 84                                |  |  |
| Units: percentage of participants |                                   |                                   |  |  |
| number (confidence interval 95%)  | 4.5 (0.56 to 15.47)               | 3.6 (0.74 to 10.08)               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Who Achieved Transfusion Avoidance up to Day 71

|   |  |
|---|--|
| End point title   | Percentage of Participants Who Achieved Transfusion Avoidance up to Day 71 |
| End point description:<br>Transfusion Avoidance was defined as participants who remained transfusion free and did not require a transfusion after the first dose of study drug through the period of interest. Percentages are based on participants with any post-baseline data for the period. For Through Day 71, only visits with data were used to assess Transfusion Avoidance. Full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab, and were not excluded from analysis. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Baseline up to Day 71   |  |

| End point values                  | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|-----------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed       | 45                                | 84                                |  |  |
| Units: percentage of participants |                                   |                                   |  |  |
| number (confidence interval 95%)  | 86.7 (73.21 to 94.95)             | 94.0 (86.65 to 98.04)             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Who Achieved Transfusion Avoidance up to Day 351

|                        |   |
|------------------------|---|
| End point title        | Percentage of Participants Who Achieved Transfusion Avoidance up to Day 351 |
| End point description: |   |

Transfusion Avoidance was defined as participants who remained transfusion free and did not require a

transfusion after the first dose of study drug through the period of interest. Denominator for a percentage was participants with at least one post-baseline data for the period. SC treated full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab SC, and were not excluded from analysis. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline up to Day 351 |           |

| End point values                  | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|-----------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed       | 44                                | 84                                |  |  |
| Units: percentage of participants |                                   |                                   |  |  |
| number (confidence interval 95%)  | 79.5 (64.70 to 90.20)             | 85.7 (76.38 to 92.39)             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Who Maintained Stabilized Hemoglobin up to Day 71

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Who Maintained Stabilized Hemoglobin up to Day 71 |
|-----------------|--|

End point description:

Stabilized hemoglobin (SHg) was defined as the avoidance of a  $\geq 2$  g/dL decrease in hemoglobin level from Baseline (defined as the last assessment prior to the first dose of the study drug) in the absence of transfusion to the end of the period of interest. Percentages were based on participants with at least one post-baseline data for the period. For Through Day 71, only visits with data were used to assess SHg. Full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab, and were not excluded from analysis. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure.

|                       |           |
|-----------------------|-----------|
| End point type        | Secondary |
| End point timeframe:  |           |
| Baseline up to Day 71 |           |

| End point values                  | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|-----------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed       | 44                                | 78                                |  |  |
| Units: percentage of participants |                                   |                                   |  |  |
| number (confidence interval 95%)  | 81.8 (67.29 to 91.81)             | 93.6 (85.67 to 97.89)             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Who Maintained Stabilized Hemoglobin up to Day 351

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Who Maintained Stabilized Hemoglobin up to Day 351 |
|-----------------|---|

End point description:

SHg was defined as the avoidance of a  $\geq 2$  g/dL decrease in hemoglobin level from SC Baseline (defined as the last assessment prior to the first dose of SC treatment) in the absence of transfusion to the end of the period of interest. Denominator for a percentage was participants with at least one post-baseline data for the period. Visits were based on the number of days since first dose of SC treatment. SC treated full analysis set included all participants who had signed informed consent, were randomized, received at least 1 dose of ravulizumab SC, and were not excluded from analysis. Here, Number of Participants analyzed signifies those participants who were evaluable for this outcome measure.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline up to Day 351

| End point values                  | Ravulizumab IV/SC Treatment Group | Ravulizumab SC/SC Treatment Group |  |  |
|-----------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed       | 44                                | 79                                |  |  |
| Units: percentage of participants |                                   |                                   |  |  |
| number (confidence interval 95%)  | 72.7 (57.21 to 85.04)             | 83.5 (73.51 to 90.94)             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to approximately 3.5 years

Adverse event reporting additional description:

Safety analysis set included all participants who received at least 1 dose of ravulizumab and were not excluded from analysis.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 26.0 |
|--------------------|------|

### Reporting groups

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Ravulizumab SC/SC Treatment Group |
|-----------------------|-----------------------------------|

Reporting group description:

During the Randomized Treatment Period, participants received a weight-based single loading dose (2400 to 2700 mg) of ravulizumab SC on Day 1, followed by maintenance weight-based doses (490 mg) of ravulizumab SC qw from Days 15 to 64. During the Extension Period (Day 71 up to Day 1275), participants received 490 mg of ravulizumab SC qw.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Ravulizumab IV/SC Treatment Group |
|-----------------------|-----------------------------------|

Reporting group description:

During the Randomized Treatment Period, participants received a weight-based single loading dose (2400 to 2700 mg) of ravulizumab IV on Day 1, followed by a maintenance weight-based dose (3000 to 3300 mg) of ravulizumab IV on Day 15. During the Extension Period (Day 71 up to Day 1275), participants received 490 mg of ravulizumab SC qw.

| Serious adverse events  | Ravulizumab SC/SC Treatment Group | Ravulizumab IV/SC Treatment Group |  |
|---|-----------------------------------|-----------------------------------|--|
| Total subjects affected by serious adverse events                   |                                   |                                   |  |
| subjects affected / exposed   | 30 / 84 (35.71%)                  | 16 / 45 (35.56%)                  |  |
| number of deaths (all causes)                                       | 2                                 | 2                                 |  |
| number of deaths resulting from adverse events                      |                                   |                                   |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                   |                                   |  |
| Basal cell carcinoma  |                                   |                                   |  |
| subjects affected / exposed   | 1 / 84 (1.19%)                    | 0 / 45 (0.00%)                    |  |
| occurrences causally related to treatment / all                     | 0 / 2                             | 0 / 0                             |  |
| deaths causally related to treatment / all                          | 0 / 0                             | 0 / 0                             |  |
| Lung adenocarcinoma   |                                   |                                   |  |
| subjects affected / exposed   | 0 / 84 (0.00%)                    | 1 / 45 (2.22%)                    |  |
| occurrences causally related to treatment / all                     | 0 / 0                             | 0 / 1                             |  |
| deaths causally related to treatment / all                          | 0 / 0                             | 0 / 0                             |  |
| Colorectal adenoma  |                                   |                                   |  |

|  |                |                |  |
|--|----------------|----------------|--|
| subjects affected / exposed                          | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Invasive ductal breast carcinoma                     |                |                |  |
| subjects affected / exposed                          | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Breast cancer metastatic                             |                |                |  |
| subjects affected / exposed                          | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Metastatic uterine cancer                            |                |                |  |
| subjects affected / exposed                          | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 1          |  |
| Renal cell carcinomas                                |                |                |  |
| subjects affected / exposed                          | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Fibroadenoma of breast                               |                |                |  |
| subjects affected / exposed                          | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| General disorders and administration site conditions |                |                |  |
| Pyrexia  |                |                |  |
| subjects affected / exposed                          | 1 / 84 (1.19%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Application site induration                          |                |                |  |
| subjects affected / exposed                          | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Malaise  |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Fatigue   |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Reproductive system and breast disorders        |                |                |  |
| Adnexal torsion                                 |                |                |  |
| subjects affected / exposed <sup>[1]</sup>      | 1 / 44 (2.27%) | 0 / 25 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pelvic pain                                     |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 3          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders |                |                |  |
| Pneumonitis                                     |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Psychiatric disorders                           |                |                |  |
| Depression                                      |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Psychiatric decompensation                      |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Injury, poisoning and procedural complications  |                |                |  |
| Procedural hypotension                          |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Transfusion reaction                            |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Immunisation reaction                           |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Ankle fracture                                  |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Femur fracture                                  |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac disorders                               |                |                |  |
| Angina pectoris                                 |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Arrhythmia                                      |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| Nervous system disorders                        |                |                |  |
| Cervicobrachial syndrome                        |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Blood and lymphatic system disorders            |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Haemolysis                                      |                |                |  |
| subjects affected / exposed                     | 5 / 84 (5.95%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 5          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Anaemia   |                |                |  |
| subjects affected / exposed                     | 2 / 84 (2.38%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 3          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Thrombocytopenia                                |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Haemolytic anaemia                              |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Neutropenia                                     |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Aplastic anaemia                                |                |                |  |
| subjects affected / exposed                     | 2 / 84 (2.38%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Febrile neutropenia                             |                |                |  |
| subjects affected / exposed                     | 2 / 84 (2.38%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Breakthrough haemolysis                         |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Eye disorders                                   |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Lens dislocation                                |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                      |                |                |  |
| Gastritis                                       |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastric haemorrhage                             |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatobiliary disorders                         |                |                |  |
| Cholecystitis acute                             |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cholecystitis                                   |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 2 / 45 (4.44%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cholangitis                                     |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cholelithiasis                                  |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Skin and subcutaneous tissue disorders          |                |                |  |
| Skin ulcer                                      |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Renal and urinary disorders                     |                |                |  |
| Urinary retention                               |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| COVID-19  |                |                |  |
| subjects affected / exposed                     | 6 / 84 (7.14%) | 2 / 45 (4.44%) |  |
| occurrences causally related to treatment / all | 0 / 6          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| Bacterial infection                             |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| COVID-19 pneumonia                              |                |                |  |
| subjects affected / exposed                     | 2 / 84 (2.38%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bacterial sepsis                                |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatitis viral                                 |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Suspected COVID-19                              |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Tubo-ovarian abscess                            |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed <sup>[2]</sup>      | 1 / 44 (2.27%) | 0 / 25 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Salmonellosis                                   |                |                |  |
| subjects affected / exposed                     | 0 / 84 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastroenteritis                                 |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Sinusitis                                       |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Osteomyelitis                                   |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Influenza                                       |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Appendicitis                                    |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Dengue haemorrhagic fever                       |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Localised infection                             |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| Urinary tract infection                         |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Anal abscess                                    |                |                |  |
| subjects affected / exposed                     | 1 / 84 (1.19%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Number exposed adjusted as this is a sex-specific event.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Number exposed adjusted as this is a sex-specific event.

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | Ravulizumab SC/SC<br>Treatment Group | Ravulizumab IV/SC<br>Treatment Group |  |
|---|--------------------------------------|--------------------------------------|--|
| Total subjects affected by non-serious adverse events |                                      |                                      |  |
| subjects affected / exposed                           | 83 / 84 (98.81%)                     | 44 / 45 (97.78%)                     |  |
| Vascular disorders                                    |                                      |                                      |  |
| Hypertension  |                                      |                                      |  |
| subjects affected / exposed                           | 3 / 84 (3.57%)                       | 3 / 45 (6.67%)                       |  |
| occurrences (all)                                     | 3                                    | 3                                    |  |
| General disorders and administration site conditions  |                                      |                                      |  |
| Injection site erythema                               |                                      |                                      |  |
| subjects affected / exposed                           | 4 / 84 (4.76%)                       | 3 / 45 (6.67%)                       |  |
| occurrences (all)                                     | 20                                   | 5                                    |  |
| Influenza like illness                                |                                      |                                      |  |
| subjects affected / exposed                           | 7 / 84 (8.33%)                       | 0 / 45 (0.00%)                       |  |
| occurrences (all)                                     | 8                                    | 0                                    |  |
| Pyrexia   |                                      |                                      |  |
| subjects affected / exposed                           | 20 / 84 (23.81%)                     | 7 / 45 (15.56%)                      |  |
| occurrences (all)                                     | 30                                   | 11                                   |  |
| Asthenia  |                                      |                                      |  |

|   |   |                       |  |
|---|---|-----------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 13 / 84 (15.48%)<br>19  | 3 / 45 (6.67%)<br>3   |  |
| Infusion site erythema<br>subjects affected / exposed<br>occurrences (all)  | 5 / 84 (5.95%)<br>23  | 1 / 45 (2.22%)<br>8   |  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)   | 7 / 84 (8.33%)<br>8   | 3 / 45 (6.67%)<br>3   |  |
| Reproductive system and breast disorders<br>Intermenstrual bleeding<br>subjects affected / exposed<br>occurrences (all) | 1 / 84 (1.19%)<br>1   | 3 / 45 (6.67%)<br>6   |  |
| Respiratory, thoracic and mediastinal disorders<br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all)         | 2 / 84 (2.38%)<br>3   | 3 / 45 (6.67%)<br>4   |  |
| Cough<br>subjects affected / exposed<br>occurrences (all)   | 6 / 84 (7.14%)<br>6   | 6 / 45 (13.33%)<br>10 |  |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)  | 6 / 84 (7.14%)<br>6   | 4 / 45 (8.89%)<br>4   |  |
| Psychiatric disorders<br>Depression<br>subjects affected / exposed<br>occurrences (all)                                 | 2 / 84 (2.38%)<br>3   | 3 / 45 (6.67%)<br>3   |  |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)   | 5 / 84 (5.95%)<br>5   | 1 / 45 (2.22%)<br>1   |  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)  | 5 / 84 (5.95%)<br>5   | 2 / 45 (4.44%)<br>2   |  |
| Product issues<br>Device delivery system issue  | Additional description: Adverse Events relating to drug delivery were coded to the MedDRA SOC of "Product Issues", including missing dose (ie, no dose) and partial dose (ie, less than full volume of dose administered) medication errors occurring with use of device. |                       |  |

|   |   |   |  |
|---|---|---|--|
| subjects affected / exposed<br>occurrences (all)  | 74 / 84 (88.10%)<br>418   | 42 / 45 (93.33%)<br>215   |  |
| Injury, poisoning and procedural complications<br>Post vaccination fever<br>subjects affected / exposed<br>occurrences (all)  | 6 / 84 (7.14%)<br>6   | 4 / 45 (8.89%)<br>4   |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Dizziness<br>subjects affected / exposed<br>occurrences (all)   | 16 / 84 (19.05%)<br>28<br><br>5 / 84 (5.95%)<br>5   | 14 / 45 (31.11%)<br>17<br><br>4 / 45 (8.89%)<br>5   |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)<br><br>Haemolysis<br>subjects affected / exposed<br>occurrences (all)<br><br>Neutropenia<br>subjects affected / exposed<br>occurrences (all)  | 12 / 84 (14.29%)<br>24<br><br>10 / 84 (11.90%)<br>17<br><br>6 / 84 (7.14%)<br>9                           | 4 / 45 (8.89%)<br>6<br><br>4 / 45 (8.89%)<br>5<br><br>2 / 45 (4.44%)<br>2                             |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Constipation<br>subjects affected / exposed<br>occurrences (all) | 17 / 84 (20.24%)<br>22<br><br>7 / 84 (8.33%)<br>7<br><br>9 / 84 (10.71%)<br>10<br><br>6 / 84 (7.14%)<br>7 | 3 / 45 (6.67%)<br>4<br><br>3 / 45 (6.67%)<br>3<br><br>5 / 45 (11.11%)<br>9<br><br>1 / 45 (2.22%)<br>3 |  |

|   |                        |                      |  |
|---|------------------------|----------------------|--|
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)  | 10 / 84 (11.90%)<br>15 | 6 / 45 (13.33%)<br>7 |  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 84 (1.19%)<br>1    | 3 / 45 (6.67%)<br>3  |  |
| Toothache<br>subjects affected / exposed<br>occurrences (all)   | 10 / 84 (11.90%)<br>12 | 4 / 45 (8.89%)<br>4  |  |
| Hepatobiliary disorders<br>Cholelithiasis<br>subjects affected / exposed<br>occurrences (all)                     | 4 / 84 (4.76%)<br>6    | 3 / 45 (6.67%)<br>3  |  |
| Skin and subcutaneous tissue disorders<br>Rash<br>subjects affected / exposed<br>occurrences (all)                | 2 / 84 (2.38%)<br>2    | 3 / 45 (6.67%)<br>3  |  |
| Renal and urinary disorders<br>Haemoglobinuria<br>subjects affected / exposed<br>occurrences (all)                | 1 / 84 (1.19%)<br>1    | 3 / 45 (6.67%)<br>3  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 7 / 84 (8.33%)<br>7    | 3 / 45 (6.67%)<br>7  |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 11 / 84 (13.10%)<br>15 | 5 / 45 (11.11%)<br>6 |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)   | 9 / 84 (10.71%)<br>10  | 5 / 45 (11.11%)<br>5 |  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)   | 7 / 84 (8.33%)<br>7    | 0 / 45 (0.00%)<br>0  |  |
| Infections and infestations   |                        |                      |  |

|                                   |                  |                  |  |
|-----------------------------------|------------------|------------------|--|
| Influenza                         |                  |                  |  |
| subjects affected / exposed       | 10 / 84 (11.90%) | 6 / 45 (13.33%)  |  |
| occurrences (all)                 | 11               | 9                |  |
| Urinary tract infection           |                  |                  |  |
| subjects affected / exposed       | 11 / 84 (13.10%) | 3 / 45 (6.67%)   |  |
| occurrences (all)                 | 19               | 3                |  |
| Upper respiratory tract infection |                  |                  |  |
| subjects affected / exposed       | 5 / 84 (5.95%)   | 3 / 45 (6.67%)   |  |
| occurrences (all)                 | 6                | 3                |  |
| Nasopharyngitis                   |                  |                  |  |
| subjects affected / exposed       | 11 / 84 (13.10%) | 8 / 45 (17.78%)  |  |
| occurrences (all)                 | 16               | 11               |  |
| COVID-19                          |                  |                  |  |
| subjects affected / exposed       | 39 / 84 (46.43%) | 16 / 45 (35.56%) |  |
| occurrences (all)                 | 42               | 18               |  |
| Paronychia                        |                  |                  |  |
| subjects affected / exposed       | 1 / 84 (1.19%)   | 3 / 45 (6.67%)   |  |
| occurrences (all)                 | 1                | 3                |  |
| Gastroenteritis                   |                  |                  |  |
| subjects affected / exposed       | 5 / 84 (5.95%)   | 5 / 45 (11.11%)  |  |
| occurrences (all)                 | 6                | 5                |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 01 August 2018    | • Removed free hemoglobin testing • Added restriction on ova donation for female subjects.   |
| 20 September 2018 | • Modified the criteria for the assessment of causality of AEs by the Investigator • Added data collection for the documentation of medication errors occurring with the use of ravulizumab on-body delivery system (OBDS) as adverse device effect (ADEs).  |
| 17 May 2019       | • Removed 3 in-clinic study visits for participants in the ravulizumab SC treatment group during the Randomized Treatment Period and replaced with self-administration of ravulizumab SC by the participant in the home setting to reduce the participants burden • Provided additional information required by International Organization for Standardization (ISO) guidelines for investigational devices • Decreased length of time on eculizumab prior to study entry from 6 months to 3 months • Decreased the period in which participant may have experienced LDH values $> 2 \times$ upper limit of normal (ULN) from 6 months to 3 months • Clarified that the quality of life (QoL) instruments will be administered and recorded on paper rather than using an e-diary. |
| 19 November 2019  | • Increased the total study treatment duration to up to 3.5 years (182 weeks) • Revised the definition for the PK analysis set based on an assessment of compliance with the dosing and PK sampling windows specified in the Schedule of Activities and on PK simulations conducted to confirm permitted dosing and sampling windows • Clarified the timing of doses and PK/PD sample collection after Day 1 • Updated definitions of overdose for ravulizumab administered via IV infusion and via the ravulizumab OBDS • Clarified the definition of ADE.  |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

To ensure quality of results, all 7 participants from a noncompliant site were excluded from all analysis sets due to source documentation deviations.

Notes: